Papahadjopoulos describes lipid:nucleic acid complexes containing, among other components: (a) a cationic lipid; (b) a nucleic acid; and (c) a hydrophilic polymer. Papahadjopoulos describes polyethylene glycol distearoyl phosphatidylethanolamine (PEG-DSPE) as an exemplary hydrophilic polymer (i.e., component (c) from the previous sentence) that can be used in the complexes disclosed therein.

The claimed microparticles differ from the complexes disclosed in Papahadjopoulos for at least the following reasons.

First, the claimed microparticles contain a polymeric "matrix" (e.g., a material in which something is enclosed or embedded). There is no indication in Papahadjopoulos that the hydrophilic polymer used therein forms a "matrix." Rather, as noted in the passage from Papahadjopoulos cited by the Examiner on page 3 of the Office Action, "the hydrophilic polymer locates and is incorporated into hydrophobic pockets" in the cationic lipid:DNA complex.

Second, Papahadjopoulos does not disclose a composition containing both the polymeric matrix and the lipid components of the claimed microparticles. It is not clear whether the Examiner alleges that PEG-DSPE in the complex of Papahadjopoulos corresponds to (i) the polymeric matrix or (ii) the lipid component of the claimed microparticle. The "polymeric matrix" and the "lipid" are two distinct components that must both be present in the claimed microparticles (claim 37 further limits claim 1 by requiring that the "lipid" be PEG-DSPE). If the Examiner asserts that PEG-DSPE in the complex of Papahadjopoulos constitutes a polymer component of the claimed microparticles, then Papahadjopoulos clearly lacks a lipid having a pKa of less than about 2.5 (Papahadjopoulos describes the inclusion of cationic lipids at, e.g., column 11, lines 1-33). If the Examiner asserts that PEG-DSPE in the complex of Papahadjopoulos constitutes a lipid component of the claimed microparticles, then Papahadjopoulos clearly lacks a polymer (Papahadjopoulos nowhere describes a complex containing both PEG-DSPE and a second "hydrophilic polymer").

Third, claim 1 requires that the claimed microparticle be less than about 100 microns in diameter. Papahadjopoulos provides no description of a non-liposome composition that would necessarily be less than about 100 microns in diameter.

In view of the foregoing, applicants respectfully submit that Papahadjopoulos does not anticipate any of claims 1-4, 6, 7, 9-16, 29, and 37.

35 U.S.C. §103(a) (Obviousness)

At pages 4-8 of the Office Action, the Examiner rejected claims 1-4, 6-16, 29, 32-34, and 37 as allegedly unpatentable over Papahadjopoulos taken with Rolland et al., U.S. Patent No. 6,040,295 ("Rolland") and further in view of Lunsford et al., U.S. Published Application No. 2002/0182258 ("Lunsford"). Similarly, at pages 9-13 of the Office Action, the Examiner rejected claims 1-4, 6, 7, 9-16, 29, 32-34, and 37 as allegedly unpatentable over Papahadjopoulos taken with Rolland and further in view of Mathiowitz et al., U.S. Patent No. 6,677,313 ("Mathiowitz").

Applicants respectfully traverse the rejection in view of the following comments.

Papahadjopoulos describes cationic lipid:nucleic acid complexes that contain at least two different "targeting moieties" attached thereto (see, e.g., abstract and column 37, lines 1-8). Targeting moieties (such as antibodies, antibody fragments, or hormones) are used by Papahadjopoulos to direct the complex to a specific cell type or location within the body. Entrapment of a targeting moiety-containing complex disclosed by Papahadjopoulos within a composition of Rolland, Lunsford, or Mathiowitz would have been expected to partially or completely mask the targeting moieties and thereby reduce or eliminate their targeting function. As a result of this expected disruption in bioactivity, the person of ordinary skill in the art would have lacked the requisite suggestion or motivation entrap a complex of Papahadjopoulos within a composition of Rolland, Lunsford, or Mathiowitz. For at least this reason, the cited references do not render obvious any of claims 1-4, 6-16, 29, 32-34, and 37.

At pages 13-15 of the Office Action, the Examiner rejected claims 21-24, 27, and 31 as allegedly unpatentable over Papahadjopoulos taken with Carson et al., U.S. Published Application No. 2003/0109469 ("Carson"), as evidenced by Adema et al., U.S. Patent No. 6,500,919 ("Adema"). Similarly, at pages 15-21 of the Office Action, the Examiner rejected

claims 21-24, 27, 28, and 31 as allegedly unpatentable over Papahadjopoulos taken with Rolland and Lunsford, and further in view of Carson, as evidenced by Adema.

Applicants respectfully traverse the rejection in view of the following comments.

The Examiner cited Carson as allegedly disclosing "employing a peptide or arrays of peptides known in the prior art in a plasmid expression vector for use as an immunogenic composition" and Adema as disclosing "MHC I binding peptides for use in vaccines." Notwithstanding the Examiner's assertions as to the disclosure of these secondary references, neither Carson nor Adema (taken alone or in combination) add what is lacking in Papahadjopoulos. As detailed above in the response to the section 102(e) rejection, the cationic lipid:nucleic acid complexes of Papahadjopoulos: (i) do not contain a polymer "matrix"; (ii) do not contain both the polymeric matrix and the lipid components of the claimed microparticles; and (iii) do not disclose a non-liposome composition that is necessarily less than about 100 microns in diameter. Similarly, as noted above in response to the section 103(a) rejection, the person of ordinary skill in the art would have lacked the requisite suggestion or motivation entrap a complex of Papahadjopoulos within a composition of Rolland or Lunsford. Carson and Adema have been cited only for their disclosure relating to immunogenic compositions and contain no teachings that would have led the person of ordinary skill in the art to modify a composition of Papahadjopoulos so as to overcome one or more of the deficiencies noted above. As a result, the cited references do not render obvious any of claims 21-24, 27, 28, and 31.

CONCLUSION

Applicants respectfully request that all claims be allowed in view of the remarks contained herein.

Enclosed is Petition for Extension of Time. Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 08191-018001.

Respectfully submitted,

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